REMARKS/ARGUMENTS

The 103 Rejections

The Examiner rejected Claims 1-13 and 15-20 under 35 U.S.C. 103(a) as being unpatentable over Wilson (US 5,756,065) in view of either one of Griffiths (WO 99/30745) or Geerlings (US 5,246,691). Applicants respectfully traverse the rejection and respond as follows.

The present application claims certain chelating agents, such as MeO-DOTA-NCS, complexed with actinium-225. Actinium-225 is an alpha emitter, having much higher energy than many other radioisotopes. The high energy of alpha emitters makes them very suitable for use with radiopharmaceuticals, but the high energy levels can also create problems with toxicity. One of the ways to reduce the toxicity problems is to complex the actinium-225 to a chelating agent which can help direct the high energy of the actinium-225 to a specific type of tissue. The chelating agents can also help to eliminate the isotope from the body so that it does not cause increased toxicity effects by accumulating in various organs throughout the body.

It is important to find a chelator that can hold or "trap" the actinium-225 sufficiently. As described in the prior art, it has historically been very difficult to find a chelating agent that is able to sufficiently form complexes with actinium-225 (see, for example, the following references that have been previously cited: Kim A. Deal et al., Improved in Vivo stability of Actinium-225 Macrocyclic Complexes, *J. Med. Chem.*, (1999), *42*, 2988-2992; Seyed K. Imam, Advancements in Cancer Therapy With Alph-Emitters: A Review, *Int. J. Radioation Oncology Biol. Phys.*, (2001) Vol. 51, No. 1, specifically p. 274; F. M. Kaspersen, et al., Cytotoxicity of ^{213}Bi- and ^{225}Ac-immunoconjugates, *Nuclear Medicine Communications*, (1995), *16*, specifically pages 468 and 475).

The Wilson reference describes compounds that form inert complexes with a metal ion selected from the group consisting of ^{153}Sm, ^{166}Ho, ^{90}Y, ^{149}Pm, ^{159}Gd, ^{140}La, ^{177}Lu, ^{175}Yb, ^{47}Sc, and ^{142}Pr (col. 6, lines 30-31), none of which are alpha emitters. Given the challenges in finding suitable chelating agents for actinium-225, as

described above, it would not be obvious that a chelating agent sufficient for use with the metals such as those described in the Wilson reference would be adequate for use with actinium-225. Therefore, claims 1-13 and 15-20 of the present application are not obvious over the Wilson reference.

The Griffiths reference describes DOTA-Biotin derivatives and does include actinium-225 in a long list of radionuclides (page 12). However, the Griffiths reference does not teach or suggest the particular chelators that are claimed in the present application. Given the challenges in forming complexes with actinium-225, as described above, it would not be obvious to select actinium-225 from the long list of radioisotopes described in Griffiths and expect that it would succesfully complex with the chelating agents of Wilson. Therefore, Claims 1-13 and 15-20 of the present application are not obvious over the Griffiths reference.

The Geerlings reference describes radioimmunotherapy using alpha particle emission and does describe the extraordinary cytotoxicity associated with alpha particles. However, the Geerlings reference does not teach or suggest the particular chelating agents claimed in the present application. Given the challenges in finding suitable chelating agents for actinium-225, as described above, it would not be obvious to substitute a different chelating agent for those described in the Geerlings reference and successfully form complexes with actinium-225. Therefore, Claims 1-13 and 15-20 of the present application are not obvious over the Geerlings reference.

Moreover, given the challenges in finding suitable chelating agents for actinium-225, it would not be obvious that the combination of Wilson, Griffths or Geerlings would work or that complexes could actually be formed through the combination of these teachings.

The Examiner rejected Claim 14 under 35 U.S.C. 103(a) as being unpatentable over Wilson in view of either one of Griffiths or Geerlings, as applied to claims 1-13 and 15-20 above, and further in view of either one of Scheinberg (XP-002194098, PTO-1449) or Co (US 5,714,350). Applicants first note that Claim 14 depends indirectly from Claim 6 and therefore contains all of the limitations of Claim 6,

including the specific chelating agents and complexes of such chelating agents with actinium-225.

The Wilson, Griffiths and Geerlings references are described above. For the reasons described above, given the challenges in finding suitable chelating agents for actinium-225, even in view of these prior art references, it would not be obvious that the particular chelating agents of claim 14 could form complexes with actinium-225.

The Scheinberg reference is a brief abstract from a conference. Scheinberg teaches complexes of CHX-A-DTPA complexed with alpha particle emitters and conjugated to specific biological molecules. Scheinberg does not teach or suggest complexes of actinium-225 with the particular chelating agents of claim 14. Therefore, Claim14 is not obvious in view of Wilson, Griffiths or Geerlings in combination with Scheinberg.

Co describes a method for increasing anitibody affinity by altering glycosylation in the immunoglobulin variable region. Co does not teach or suggest complexes of chelating agents with with actinium-225 as is claimed in Claim 14. Therefore, Claim14 is not obvious in view of Wilson, Griffiths or Geerlings in combination with Co.

For all of these reasons, the claims of the present invention are not obvious over Wilson, Griffiths, Geerlings, Scheinberg or Co, either alone or in combination.

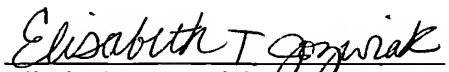
The 112 rejections

The Examiner rejected Claim 12 under 35 U.S.C. 112, second paragraph, stating that the recitation of "NuM195" is unclear. Applicants would like to thank the Examiner for pointing out this typographical error, which has been corrected in the amended claims.

Conclusion

In view of the foregoing amendments and remarks, Applicants believe the present application now stands in condition for allowance. Early notification thereof is respectfully requested.

Respectfully submitted,



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